Evolutionary Adaptations of Intracranial Pressure to Gravity

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The microgravity environment of spaceflight removes hydrostatic pressure gradients within the human body that are associated with upright posture on Earth. Exposure to microgravity causes a blood shift from legs toward the head, which probably elevates carotid arterial pressure and jugular venous pressure. These factors may elevate intracranial pressure (ICP), cause headache, nausea, and vomiting, and reduce crew performance in orbit. When astronauts return to Earth, about half are unable to stand upright, which may be caused by a combination of blood volume loss, leg muscle loss, and altered baroreflex control of blood pressure and flow to the head. It is important to investigate gravitational effects on ICP from a fundamental biological standpoint.

Snakes provide sensitive animal models for studying cardiovascular adaptation because of their long body form and diversification of behavioral ecology. They also provide sensitive models for investigating ICP regulation with altered posture. In general, arboreal snakes are tolerant against gravitational stress, whereas aquatic snakes have less ability to resist gravitational stress. Presently there is no knowledge of how species from differing gravitational habitats deal with postural effects in terms of their ICP. Therefore, the purpose of this study was to evaluate the gravitational adaptation of ICP in snakes.

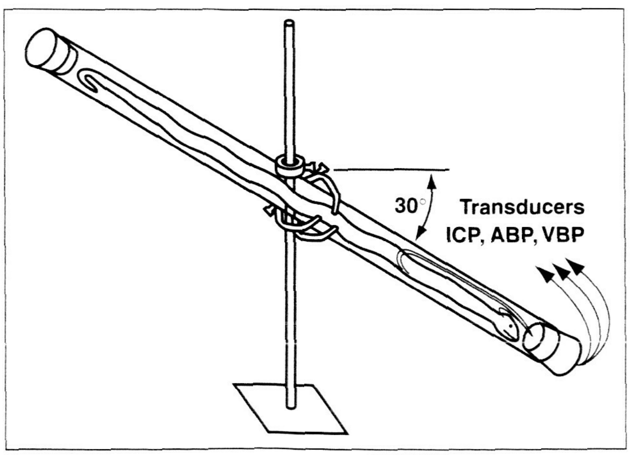

Fig. 1. Drawing of a head-down tilted snake inside the tube. ICP = intracranial pressure, ABP = arterial blood pressure, VBP = venous blood pressure.

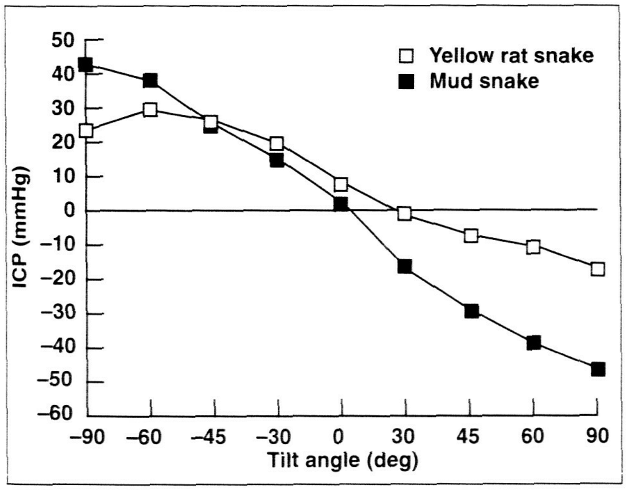

Fig. 2. In the mud snake (aquatic species), ICP increased to 42 millimeters mercury (mmHg) during head-down tilt, whereas in the yellow rat snake (semi-arboreal species), ICP rose to 23 mmHg.

In these studies yellow rat snakes (*Elaphe obsoleta*) represented a semi-arboreal species, and mud snakes (*Farameia abacura*), an aquatic species. Catheters were placed in their right aortic arch, inferior vena cava, and intracranial space in order to measure aortic blood pressure, venous blood pressure, and ICP simultaneously. After surgery, the snakes were confined within an individually-fitted clear acrylic tube and were tilted from 0 degrees (horizontal) to the following angles: 30, 45, 60, and 90 degrees as shown in the first figure. Each angle was held for two minutes. Comparisons of the investigated parameters were made between these two species with contrasting gravity exposure during their respective evolutionary histories.

During head-down tilt in aquatic snakes, ICP increased more rapidly and to higher levels than that in arboreal snakes as shown in the second figure. Compared to arboreal snakes, aquatic snakes have limited ability to counteract gravitational stress by preventing rapid elevations and high levels of ICP in head-down tilt postures. These results help the investigators understand how microgravity affects cerebral circulation and fluid balance in an evolutionary context. Furthermore, snakes may provide an excellent model for contrasting the long-term effects of gravity adaptation (arboreal snakes) versus microgravity adaptation (aquatic snakes) on the cardiovascular system.

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Calcium Metabolism in Bion 11 Monkeys

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The calcium endocrine system regulates the supply of calcium and phosphorus for the mineralization of bone, a process that is known to be depressed during spaceflight. The role of circulating hormones in the localized decrease in bone formation in the weight-bearing skeleton is unresolved and difficult to study in the human because of the effects of exercise itself on calcium metabolism. Additional knowledge would not only improve understanding of the mechanism of adaptation to a weightless environment, but also provide a rationale for the use of the hormones of the calcium endocrine system—parathyroid hormone, calcitonin, and the vitamin D hormone (1,25-D)—in the prevention or restoration of bone loss during spaceflight. Currently, therapeutic trials that include these hormones are under way for the human osteoporoses that can result from systemic factors such as estrogen deficiency.

The Bion mission provided the opportunity to examine the effects of spaceflight on the circulating levels of calcium regulating hormones in rhesus monkeys. Bone tissue obtained by iliac-crest biopsy showed clear effects of weightlessness in flight animals, but not in chair-restrained ground controls.

The calcium endocrine study required validation of the human assays used to measure the peptide hormones, parathyroid hormone, and calcitonin because of structural differences in monkey and human hormones. Validation involved the assay of blood samples obtained before and after a 10-minute calcium infusion, and confirmation of the physiologic response. Assays in the laboratory of Dr. Leonard Deftos from the University of California, San Diego, were successful in showing increases in calcitonin, and decreases in parathyroid hormone after calcium infusion, as illustrated in panels A and B of the first figure.

The third hormone of the calcium endocrine system is a sterol that circulates in the rhesus monkey in concentrations seven to ten times higher than in man. To evaluate changes in the levels during spaceflight, serum 1,25-D was monitored during the development of vitamin D deficiency, induced by removing diet sources of vitamin D and exposure to sunlight for four months. The hormone decreased 30, 48, and 83% from basal levels after 1, 2, and 4 months, respectively.

The most striking changes during the 17-day spaceflight were observed in the concentration of vitamin D hormone, which decreased from 75% to 68% in the serum of flight monkeys, and from 27% to 73% (average 54%) in five ground controls, as illustrated in the second figure. At the whole body level, this hormone functions to facilitate calcium transport in the intestine, kidney, and bone, and to differentiate bone cells. Theoretically, a decrease in the level of circulating hormone would not only reduce intestinal calcium and phosphorus absorption, but also indirectly reduce bone resorption. This might be considered an appropriate physiologic response for an unloaded, inactive skeleton, a view that is supported by results from a human bed-rest study in which isokinetic exercise which loaded bone prevented both a decrease in serum 1,25-D, and an increase in urinary calcium excretion. The spaceflight response was not greater than the response on Earth, an indication that the endocrine regulation of